Role of Platelet Rich Fibrin in Healing of Extraction Socket

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ABSTRACT

Introduction: Platelet Rich Fibrin (PRF) consists of an autologous leukocyte-platelet-rich fibrin matrix composed of a tetra molecular structure, with cytokines, platelets, cytokines, and stem cells within it which acts as a biodegradable scaffold that favors the development of microvascularization and is able to guide epithelial cell migration to its surface. This clinical study was designed to evaluate the role of Platelet Rich Fibrin in terms of healing and bone regeneration potential in extraction sockets and its comparison with the naturally healing socket.

Material and methods: The study conducted at Oral and Maxillofacial Surgery, VSPM's dental college Nagpur, during year January 2012 to December 2014 with defined inclusion and exclusion criteria. The enrolled 120 participants For evaluation of extraction wound healing of Platelet rich fibrin gel and the control group on RVG, bone density was measured and compared STATA Version 10.0 was used for statistical analysis.

Results: Mean bone density (grey scale/ pixels) of PRF group after 24 week was significantly high 119.60± 7.43 for maxilla and 135.62± 9.90 for mandible as compare to control. 105.33± 6.35 for maxilla 123.36± 5.65 for mandible.

Conclusion: Platelet rich fibrin appears as a satisfactory alternative with favorable results and low risks in extraction sockets healing.

Keywords: Autologus, Bone Density, Bioactive Surgical Additives, Exodontias, Mandible, Maxilla, Radio Visuo Graphy Wound Healing

INTRODUCTION

Wound healing is an intricate and complex process and is susceptible to interruption or failure leading to delayed healing or non healing wounds. It is a highly orchestrated event and a proper wound care is essential to enhance the healing process. The development of bioactive surgical additives has evolved a great challenge in clinical research. Bioactive surgical additives help to regulate inflammation and increase the speed of healing process.[1] Various signalling proteins mediate the process of healing of both hard and soft tissues by regulating the cascade of intracellular and extracellular events.

There are several allografts, xenograft or alloplastic graft materials commonly used for bone regeneration procedures like freeze dried bone grafts, demineralised freeze dried bone grafts, hydroxyapatite, bioactive glass etc. which have shown to possess good osteoinductive and osteoconductive properties, but the risk of disease transmission and unpredictable outcome many a times, led to search of materials which can independently produce predictable regeneration or can improve properties of these graft materials.[2]

Platelets have been shown to play a crucial role in wound healing.[1] Platelets are known to release a variety of growth factors like Platelet-derived growth factor (PDGF), Epidermal growth factor (EGF), Transforming growth factor (TGF-beta), Fibroblast growth factor (FGF),Vascular endothelial growth factor (VEGF), Insulin –like growth factors (IGF-I) which hasten up the healing process.

The advent of different platelet concentrate technologies gave a way to development of new kind of fibrin adhesive, concentrated platelet-rich plasma (cPRP). Because of legal restrictions on blood handling, a new family of platelet concentrate, which is neither fibrin glue nor a classical platelet concentrate, appeared in France. This new biomaterial, called platelet-rich fibrin (PRF) was developed by Choukroun et al in 2001. Since then Chokroun's PRF has found clinical applications in bone reconstruction procedures (Mazor et al 2009), treating residual extraction sockets[3] and for root coverage in case of gingival recession.[4]

In this randomized clinical trial, an attempt was made to evaluate the role of Platelet Rich Fibrin(PRF) in terms of healing and bone regeneration potential in extraction sockets and its comparison with the naturally healing extraction socket wound.

MATERIAL AND METHODS

The present study was undertaken at the department Oral and Maxillofacial Surgery, VSPM's dental college Nagpur, during year January 2012 to December 2014 after obtaining ethical clearance from the Institutional Ethics Committee. This study involved both male and female patients, who were referred to the department of Oral and Maxillofacial Surgery for extraction of tooth. Complete history of all the patients was taken and thorough clinical examination and

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investigation was done to rule out any systemic problem.

Inclusion criteria: All Patients in the age group 18 years and 40 years, under ASA 1 undergoing exodontia procedures and those who agreed to be part of the study protocol.

Exclusion criteria: All Patients with contraindication for local anaesthesia or surgery, periodontally compromised patients, those with uncontrolled medical conditions, platelet disorders or patients with history of platelet disorders and those having deleterious habits (tobacco/kharra/khaini chewing and smokers)

A total of 120 patients were included in the study and randomly distributed into 2 groups with 60 patients each. All the participants were informed before their participation in the study and written informed consent were taken for procedure, photographs and publication.The disclosure of privacy of the identity has been explained, although none of the participants privacy has been disclosed.

Group 1: PRF placed into the extraction socket

This group was further sub divided into 2 subgroups Maxilla and Mandible, each having 30 extraction sockets in respective sub groups.

Group 2: Control group with no bio-additives

Similar to group 1, it was further sub divided into 2 subgroups Maxilla and Mandible, each having 30 extraction sockets in respective sub groups.

Procedure: Following appropriate intraoral nerve blocks in accordance to the indicated tooth with 2% solution of lignocaine hydrochloride and 1:2,00,000 adrenaline, extraction of the tooth was performed using suitable instruments and technique as per the requirement. After thorough debridement, the socket was made ready for receiving PRF gel (group 1). Till the time of fabrication of PRF gel, socket was packed with sterile gauze temporarily.

Preparation of PRF gel:

10 ml of the venous blood was withdrawn from the peripheral veins of the upper limb and collected in a pre sterilized test tube without an anticoagulant and centrifuged immediately at 3000 rpm (approx) for 10 minutes. The PRF clot so formed was retrieved from the test tube, and immediately placed in empty extraction socket. Primary closure was done with 3-0 mersilk suture.

In group 2 i.e. control group (with no bio additives), the extraction socket was thoroughly debrided followed by primary closure with 3-0 mersilk suture/pack.

The patients were informed regarding the routine post operative care followed by suture removal on the seventh post operative day.

For evaluation of extraction wound healing of PRF gel and the control group on RVG, bone density was measured and compared (using Digora Optiprime Digital software 2.5 version) at following intervals: on day of extraction, 6 weeks after extraction, 12 weeks after extraction, 18 weeks after extraction, 24 weeks after extraction.

RESULTS

For PRF group; mean age ± SD for maxilla sub group was 28.16± 5.36 and for Mandible it was 27.5± 6.09. For control group; mean age ± SD for maxilla sub group was 29.36± 6.17 and for Mandible it was 28.0± 6.78. (Table1)

The mean bone density between Male and Female in Mandibular bone both the PRF and the control group combined. At all the intervals of the follow-up there was significantly high value for the mean bone density in male

Time of Follow up	PRF Mean ± SD	Control Mean ± SD	p-value
0 day	57.43 ±3.42	56.26± 3.48	0.1963, NS
6 wks	60.37± 3.31	58.30 ±3.68	0.0263, S
12 wks	85.60± 5.15	75.52 ±5.55	<0.0001, HS
18 wks	110.30 ±6.78	100.43± 6.67	<0.0001, HS
24 wks	119.60± 7.43	105.33± 6.35	<0.0001, HS
F-value	564.6	497.6	
p-value	<0.0001, HS	<0.0001, HS	

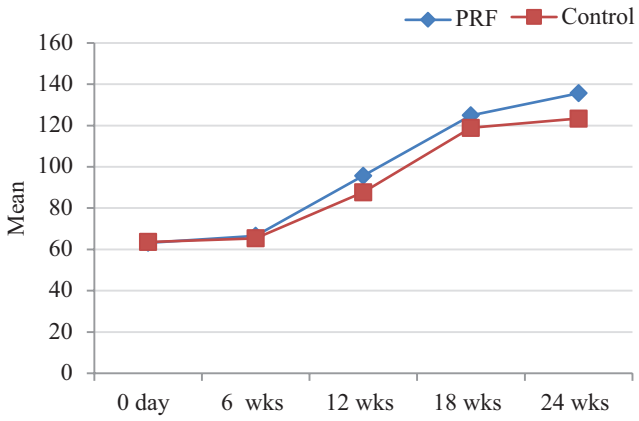
Table-1: Mean and SD value of bone density (grey scale/ pixels) at different time point in PRF and Control group in Maxilla

Time Of Follow Up	Maxilla Mean Bone Density ±SD	Mandible Mean Bone Density ±SD	p-value
0 day	57.43± 3.42	63.71± 2.96	<0.0001, HS
6 wks	60.37± 3.32	66.57± 3.39	<0.0001, HS
12 wks	85.60± 5.15	95.67± 6.98	<0.0001, HS
18 wks	110.30± 6.78	124.92± 8.73	<0.0001, HS
24 wks	119.60± 7.43	135.62± 9.90	<0.0001, HS

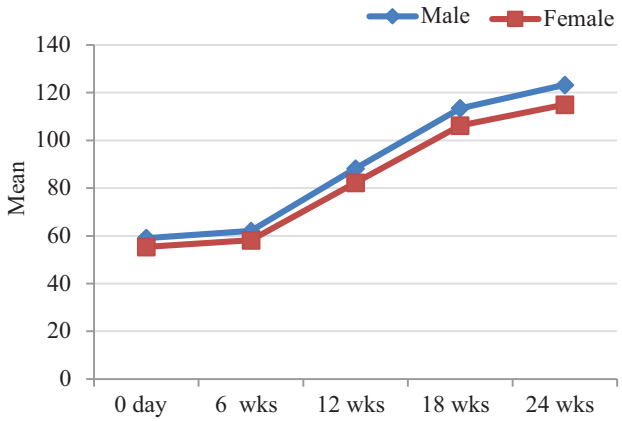
Table-2: Mean bone density (grey scale/ pixels) of PRF group at different time point between Maxilla and Mandible

Time Of Follow Up	Maxilla Mean Bone Density ±SD	Mandibular Mean Bone Density ±SD	p-value
0 day	56.26 ±3.48	63.61± 2.19	<0.0001, HS
6 wks	58.30± 3.68	65.38 ±2.07	<0.0001, HS
12 wks	75.52± 5.55	87.71± 3.96	<0.0001, HS
18 wks	100.43 ±6.67	118.9 ±5.60	<0.0001, HS
24 wks	105.33± 6.35	123.36± 5.65	<0.0001, HS

Table-3: Mean bone density (grey scale/ pixels) of Control group at different time point between Maxilla and Mandible



Graph-1: Changes in bone density at different time point in PRF and Control group of Mandible



Graph-2: Mean bone density between Male and Female in Maxilla

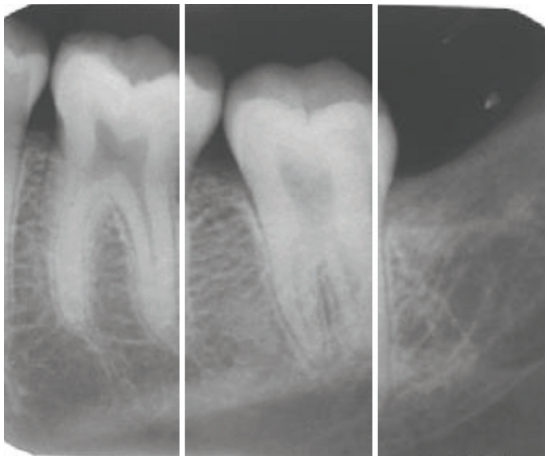


Figure-1: Bone density at 24week in control group

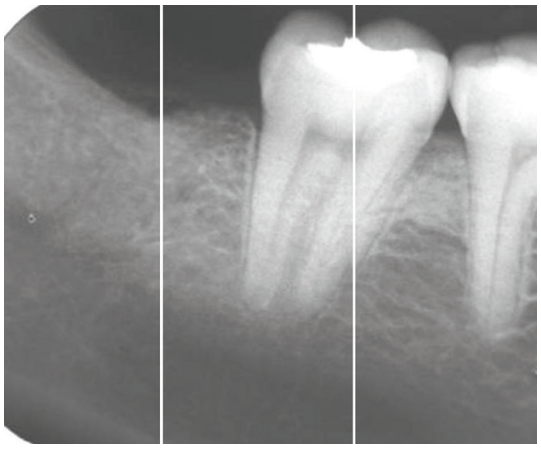


Figure-2: Bone density at 24week in PRF group

gender as compared to the females.

Radiographic evaluation of the bone density (grey scale/ pixels) using the RVG (Digora Optiprime software) was done at subsequent follow-ups viz. 0 day, 6 weeks, 12 weeks, 18 weeks and 24 weeks. (Figure 1and 2)

Mean bone density (grey scale/ pixels) at different follow-ups (time point) were compared by performing Repeated Measure ANOVA test. Changes in mean bone density (grey scale/ pixels) at different follow-ups (time point) between PRF and Control group were compared by unpaired t-test. $p<0.05$ was considered as statistically significant. Statistical Software STATA Version 10.0 was used for statistical analysis. The mean bone density at 6 week for mandible in combined group was (60.37± 3.31) in PRFgroup seen, which was significantly high as compare to control(58.30 ±3.68) ($p<0.05$).The results were again highly significant after 24 week when assessd, i.e. 119.60± 7.43 with PRF as compare to control (105.33± 6.35) ($p<0.001$) (Table 3)

The Mean bone density (grey scale/ pixels) of PRF group at different time point between Maxilla and Mandible also compared and we found 119.60± 7.43 for maxilla and 135.62± 9.90 for mandible as compare to control. 105.33± 6.35 for maxilla 123.36± 5.65 for mandible.

The results of the present study indicated that there was early osseous regeneration in the PRF group as compared to the control group at a given point of time in maxillary as well as mandibular bone in both the genders, the difference being statistically significant.

DISCUSSION

Since years, several allografts, xenograft or alloplastic graft materials are being commonly used for bone regeneration procedures. They include freeze dried bone grafts, demineralised freezed dried bone grafts, hydroxyapatite, bioactive glass etc. These biologically active materials are said to possess good osteoinductive and osteoconductive properties, but risk of disease transmission and unpredictable outcome many a times, led to search of materials which can independently produce predictable regeneration or can improve properties of these graft materials.[2]

Platelet rich fibrin was first described by Choukroun et al. in France. It has been referred as second generation platelet concentrate, PRP being the first. Dohan and Diss presented a report of clinical trials comparing the growth factor content of PRP and PRF at the Second International Symposium on growth factors in May 2006.[5] Combining the growth factors has been shown to accelerate bone repair and promote fibroblast proliferation, and increase tissue vascularity, rate of collagen formation, mitosis of mesenchymal stem cells and endothelial cells, as well as osteoblasts, playing key roles in the rate and extent of bone formation.[4]

PRF is in the form of a platelet gel and can be used in conjunction with bone grafts, which promotes wound healing, bone growth and maturation, graft stabilization, wound sealing and hemostasis and improves the handling properties of graft materials. PRF can also be used as a membrane. Clinical trials suggest that the combination of bone grafts and growth factors contained in PRP and PRF may be suitable to enhance bone density.[6]

The chief advantages of PRF over PRP are no biochemical handling of blood (strictly autologous), simplified and cost-effective process, no requirement of use of bovine thrombin and anticoagulants, favorable healing due to slow polymerization, more efficient cell migration and proliferation, supportive effect on immune system, helps in hemostasis.[7] Hence, in the present study, PRF was preferred over PRP.

Choukroun J et al, 2006 published an article describing the

method of preparation of PRF without an anticoagulant. Because of the absence of an anticoagulant, blood begins to coagulate as soon as it comes in contact with the glass surface. Therefore, for successful preparation of PRF, speedy blood collection and immediate centrifugation, before the clotting cascade is initiated, is absolutely essential. In the present study, Choukroun's method was used for the fabrication of the PRF gel since this method was simple, less technique sensitive, without use of chemical additives and less time consuming.

In the present study, a total of 120 patients were selected for the study and divided into 2 groups - group 1 was the PRF or the test group group 2 was the Non PRF group or the control group with 60 subjects in each group. Each group was further sub divided into 2 subgroups: sub group A comprising of 30 maxillary extraction sockets and sub group B having 30 mandibular sockets. The results of our study indicated that there was early osseous regeneration in the study group as compared to the control group at a given point of time in maxillary as well as mandibular bone in both the genders (graph no.1 and graph no. 2). This was attributed to the better biological properties of PRF. This was in agreement to the results obtained in previous studies conducted by B.I. Simon et al 2009 and Ziv Mazor et al 2009.[3,8]

Also in this research, a comparison was made between the mean bone density in both the genders in Maxillary as well as Mandibular bone, both the PRF and the control group combined. At all the intervals of the follow-up there was significantly high value for the mean bone density in male gender as compared to the females.The results of our study were in accordance with the previous studies by Nieves JW et al 2005 and Avdagić SC et al 2009.[9,10]

The third aspect studied in this research was the mean bone densities observed in male and female subjects, at different time intervals during follow up in Maxillary as well as Mandibular bone, both PRF and control group combined. The results of the present study indicated that at all the intervals i.e. follow ups there was significantly higher mean bone density of mandible as compared to maxilla. (Table no.1 and 2). This was in conformity to the results obtained in previous studies by Devlin H et al 1998, Park H S et al 2008, A Gulsahi et al 2010.[11,12,13]

CONCLUSION

The study clearly indicates PRF to be a promising biomaterial for definite improvement and faster regeneration of bone after exodontia procedure. This improvement with increase in the bone density signifies and highlights the use of autologous PRF, certainly as a valid method in inducing and accelerating hard tissue regeneration. The slow polymerization mode confers to PRF membrane as a particularly favourable physiologic architecture to support the healing process. Future studies regarding the inflammatory property of this material and also further clinical trials with longer duration follow up, with larger sample size and precise bone density measurement tools should be done to get more affirmative and conclusive results.

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REFERENCES

1. Dohan DM, Choukroun J,Diss A,Dohan SL,Dohan AJ,Mouhyi J,et al. Platelet-rich fibrin(PRF): A second-generation platelet concentrate,Part I:Technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:E37-44
2. Sunitha Raja V, Munirathnam Naidu E. Platelet-rich fibrin: evolution of a second-generation platelet concentrate. Indian J Dent Res. 2008;19:42-6
3. Mazor Z, Horowitz RA, Del Corso M, Prasad HS, Rohrer MD, Dohan Ehrenfest DM. Sinus floor augmentation with simultaneous implant placement using Choukroun's platelet-rich fibrin as the sole grafting material: a radiologic and histologic study at 6 months. J Periodontol. 2009;80:2056-64.
4. Anilkumar K, Geetha A, Umasudhakar, Ramakrishnan T, Vijayalakshmi R, Pameela E. Platelet-rich-fibrin: A novel root coverage approach. J Indian Soc Periodontol. 2009;13:50-4.
5. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, Dohan AJ, Mouhyi J, Dohan DM. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part IV: Clinical effects on tissue healing.Oral Surg Oral Med Oral Pathol Oral Radiol Endod.2006;101:e56-60
6. Sánchez AR, Sheridan PJ, Kupp LI. Is platelet-rich plasma the perfect enhancement factor? A current review. Int J Oral Maxillofac Implants. 2003;18:93-103.
7. Toffler M, Toscano N, Holtzclaw D, Corso MD, Dohan Ehrenfest DM.Introducing Choukroun's platelet rich fibrin (PRF) to the reconstructive surgery milieu. J Implant Adv Clin Dent 2009;1:21-30.
8. Simon BI, Zatcoff AL, Kong JJ, O'Connell SM. Clinical and Histological Comparison of Extraction Socket Healing Following the Use of Autologous Platelet-Rich Fibrin Matrix (PRFM) to Ridge Preservation Procedures Employing Demineralized Freeze Dried Bone Allograft Material and Membrane.Open Dent J. 2009;3:92-9.
9. Nieves JW, Formica C, Ruffing J, Zion M, Garrett P, Lindsay R, Cosman F. Males have larger skeletal size and bone mass than females, despite comparable body size. J Bone Miner Res. 2005;20:529-35.
10. Avdagić SC, Barić IC, Keser I, Cecić I, Satalić Z, Bobić J, Gomzi M. Differences in peak bone density between male and female students. Arh Hig Rada Toksikol. 2009;60:79-86.
11. Devlin H, Horner K, Ledgerton D. A comparison of maxillary and mandibular bone mineral densities. J Prosthet Dent. 1998;79:323-7.

12. Park HS, Lee YJ, Jeong SH, Kwon TG. Density of the alveolar and basal bones of the maxilla and the mandible. Am J Orthod Dentofacial Orthop. 2008;133:30-7.
13. A Gulsahi, CS Paksoy and Y Genc Assessment of bone mineral density in the jaws and its relationship to radiomorphometric indices. Dentomaxillofac Radiol. 2010;39:284-289.

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